

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Axel ULLRICH et al.  
Title: FLK-1 IS A RECEPTOR FOR VASCULAR ENDOTHELIAL  
GROWTH FACTOR  
Prior Appl. No.: 09/766,678  
Prior Appl. Filing Date: January 23, 2001  
Examiner: Unassigned  
Art Unit: Unassigned

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Mail Stop PATENT APPLICATION  
Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Applicants submit herewith on Form PTO/SB/08 a listing of the documents cited by or submitted to the U.S. PTO in parent application Serial No. 09/766,678, filed 01/23/2001; which is a continuation of application Serial No. 08/965,598, filed 11/06/1997, which is a continuation of 08/193,829, filed 02/09/1994, which is a continuation-in-part of application Serial No. 08/038,596, filed 03/26/1993, which is a continuation-in-part of application Serial No. 07/975,750, filed 11/13/1992. As provided in 37 CFR §1.98(d), copies of the documents are not being provided since they were previously submitted to the United States Patent & Trademark Office in the above-identified parent application.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date 10 March 2004

By 

FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 672-5475  
Facsimile: (202) 672-5399

Beth A. Burrous  
Attorney for Applicant  
Registration No. 35,087

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO  
**INFORMATION DISCLOSURE  
 STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 4

**Complete if Known**

Prior Application Number 09/766,678  
 Prior Appl. Filing Date 01/23/2001  
 First Named Inventor Axel ULLRICH et al.  
 Group Art Unit Unassigned  
 Examiner Name Unassigned  
 Attorney Docket Number 034536-1243

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
/LS/	A1	5,185,438		LEMISHKA	02-08-1993	
	A2	5,712,395		APP et al.	01-27-1998	
	A3	5,763,441		APP et al.	06-09-1998	
	A4	5,766,860		TERMAN et al.	06-16-1998	
	A5	5,792,771		APP et al.	08-11-1998	
	A6	5,792,783		TANG et al.	08-11-1998	
	A7	5,851,999		ULLRICH et al.	12-22-1998	
	A8	5,869,742		KÖSTER et al.	02-09-1999	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	1 <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
/LS/	A9	WO	92/03459	A1	SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH	03-05-1992		
	A10	WO	92/14748	A1	AMERICAN CYANAMID COMPANY	09-03-1992		
	A11	WO	92/17486	A1	TRUSTEES OF PRINCETON UNIVERSITY	10-15-1992		
	A12	WO	94/10292	A1	NEUROSPHERES LTD.	05-11-1994		
	A13	WO	95/21868	A1	IMCLONE SYSTEMS INCORPORATED	08-17-1995		
	A14	WO	96/20403	A1	LUDWIG INSTITUTE FOR CANCER RESEARCH	07-04-1996		

Examiner Signature

Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO  
**INFORMATION DISCLOSURE  
 STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 2 of 4

**Complete if Known**

Prior Application Number	09/766,678
Prior Appl. Filing Date	01/23/2001
First Named Inventor	Axel ULLRICH et al.
Group Art Unit	Unassigned
Examiner Name	Unassigned
Attorney Docket Number	034536-1243

**OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
/LS/	A15	BREIER et al., "Expression of Vascular Endothelial Growth Factor During Embryonic Angiogenesis and Endothelial Cell Differentiation," <u>Development</u> 114:521-532, 1992.	
	A16	CONN et al., "Purification of a Glycoprotein Vascular Endothelial Cell Mitogen From a Rat Glioma-derived Cell Line," <u>Proc. Natl. Acad. Sci. USA</u> 87:1323-1327, 1990.	
	A17	CONNOLLY et al., "Human Vascular Permeability Factor. Isolation from U937 Cells," <u>The Journal of Biological Chemistry</u> , Vol. 264, No. 33, p.20021, (25 November 1989).	
	A18	De VRIES et al., "The <i>fms</i> -Like Tyrosine Kinase, a Receptor for Vascular Endothelial Growth Factor," <u>Science</u> 255:989-991, 1992.	
	A19	FERRARA et al., "Pituitary Follicular Cells Secrete a Novel Heparin-Binding Growth Factor Specific for Vascular Endothelial Cells," <u>Biochem. Biophys. Res. Comm.</u> 161:851-858, 1989.	
	A20	FERRARA et al., "The Vascular Endothelial Growth Factor Family of Polypeptides," <u>J. Cell Biochem.</u> 47:211-218, 1991.	
	A21	GOSPODAROWICZ et al., "Isolation and Characterization of a Vascular Endothelial Cell Mitogen Produced by Pituitary-Derived Folliculo Stellate Cells," <u>Proc. Natl. Acad. Sci. USA</u> 86:7311-7315, 1989.	
	A22	KASHLES et al., "A Dominant Negative Mutation Suppresses the Function of Normal Epidermal Growth Factor Receptors by Heterodimerization," <u>Mol. Cell. Biol.</u> 11:1454-1463, 1991.	
	A23	KLGSBURN et al., "Regulators of Angiogenesis" <u>Annu. Rev. Physiol.</u> 53:217-39, 1991.	
	A24	LEUNG et al., "Vascular Endothelial Growth Factor Is a Secreted Angiogenic Mitogen," <u>Science</u> 246:1306-1309, 1989.	
	A25	Li et al., "Monoclonal antibodies to recombinant human vascular endothelial growth factor (rHuVEGF)," <u>Journal of Cellular Biochemistry</u> , vol. Suppl., no. 15F, p.251, (1991).	
	A26	LIVNEH et al., "Reconstitution of human epidermal growth factor receptors and its deletion mutants in cultured hamster cells," <u>J. Biol. Chem.</u> 261(27):12490-12497, 1986.	
	A27	MAGLIONE et al., "Isolation of Human Placental cDNA Coding For a Protein Related to the Vascular Permeability Factor," <u>Proc. Natl. Acad. Sci. USA</u> 88:9267-9271, 1991.	
	A28	MATTHEWS et al., "A Receptor Tyrosine Kinase cDNA Isolated From a Population of Enriched Primitive Hematopoietic Cells and Exhibiting Close Genetic Linkage to <i>c-kit</i> ," <u>Proc. Natl. Acad. Sci. USA</u> 88:9026-9030, 1991.	

Examiner  
Signature

Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST 3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449B/PTO  
**INFORMATION DISCLOSURE  
 STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 3 of 4

**Complete if Known**

Prior Application Number	09/766,678
Prior Appl. Filing Date	01/23/2001
First Named Inventor	Axel ULLRICH et al.
Group Art Unit	Unassigned
Examiner Name	Unassigned
Attorney Docket Number	034536-1243

**OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
/LS/	A29	McCORMICK, "Human gene therapy: The first round," <u>Biotechnology</u> 3(8):689-693, 1985.	
	A30	McMAHON et al., "Protein kinase inhibitors: structural determinants for target specificity," <u>Current Opinions in Drug Discovery and Development</u> 1(2):131-146, 1998.	
	A31	MILLAUEUR et al., "High affinity VEGF binding and developmental expression suggest Flk-1 as a major regulator of vasculogenesis and angiogenesis," <u>Cell</u> 72:835-846, 1993.	
	A32	MITCHELL et al., "Recombinant Expression and Characterization of the 121 Amino Acid Form of Vascular Endothelial Growth Factor (VEGF)," <u>J. Cell. Biochem., Keystone Symposia on Molecular and Cellular Biology</u> , Supplement 15C, Excerpt G207, 1991.	
	A33	NICOLAS et al., "Retroviral Vectors," <u>Vectors</u> , Chapter 25, pp. 493-494, 1987.	
	A34	ORKIN et al., "Report and Recommendations of the panel to assess the NIH investment in research on gene therapy", December 7, 1995.	
	A35	PLATE et al., "Up-Regulation of Vascular Endothelial Growth Factor and Its Cognate Receptors in a Rat Glioma Model of Tumor Angiogenesis," <u>Cancer Research</u> 53:5822-5827, 1993.	
	A36	PRYWES et al., "Mutations in the cytoplasmic domain of EGF receptor affect EGF binding and receptor internalization," <u>EMBO J.</u> 5(9):2179-2190, 1986.	
	A37	RISAU et al., "Changes in the Vascular Extracellular Matrix During Embryonic Vasculogenesis and Angiogenesis," <u>Development Biology</u> 125:441-450, 1988.	
	A38	SARZANI et al., "A Novel Endothelial Tyrosine Kinase cDNA Homologous To Platelet-Derived Growth Factor Receptor cDNA" <u>Biochem. Biophys. Res. Comm.</u> 186:706-714, 1992.	
	A39	SPIVAK-KROIZMAN et al., "Heterodimerization of c-erbB2 With Different Epidermal Growth Factor Receptor Mutants Elicit Stimulatory or Inhibitory Responses," <u>J. Biol. Chem.</u> 267:8056-8063, 1992.	
	A40	STRAWN et al., "Flk-1 as a Target for Tumor Growth Inhibition," <u>Cancer Research</u> 56:3540-3545, 1996.	
	A41	TARTAGLIA et al., <u>J. Biol. Chem.</u> 267(7), 4304-4307, March 5, 1992.	
▼	A42	TERMAN et al., "Identification of a New Endothelial Cell Growth Factor Receptor Tyrosine Kinase," <u>Oncogene</u> 6:1677-1683, 1991.	

Examiner  
Signature

Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor precedes the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

number.

**Complete if Known**

(use as many sheets as necessary)

<b>Prior Application Number</b>	09/766,678
<b>Prior Appl. Filing Date</b>	01/23/2001
<b>First Named Inventor</b>	Axel ULLRICH
<b>Group Art Unit</b>	Unassigned
<b>Examiner Name</b>	Unassigned
<b>Attorney Docket Number</b>	034538-1243

Sheet 4 of 4

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

[illegible]

Examiner  
Signature

/Lorraine Spector/

Date Considered

04/11/2007

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST 3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>8</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>9</sup>Applicant is to place a check mark here if English language Translation is attached.

**Burden Hour Statement:** This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.